REMARKS

Applicants have amended claims 10, 12, 13, and 14 to promote clarity. In particular, amended claim 13 now recites "an antigenic gene," which is consistent with the intended use of a Lac shuttle vector as a vaccine carrier. No new matter has been introduced by the amendment. Specifically, support for amendment to claim 13 can be found, e.g., at page 3, last paragraph, of the specification.

Claims 1-14 are currently pending. Reconsideration of this application, as amended, is respectfully requested in view of the remarks below.

Rejection under 35 U.S.C. § 112, first paragraph

Claims 1-14 remain rejected under 35 U.S.C. § 112, first paragraph for non-enablement on two grounds, each of which is respectfully traversed as follows:

I

Claim 1 is drawn to a Lac shuttle vector that contains various regulatory sequences, a gene to be expressed, a lactic acid bacterial plasmid sequence, and a non-antibiotic marker gene.

Claim 1 remains rejected by the Examiner for lack of enablement. Specifically, the Examiner asserted that the **only use** for a Lac shuttle vector, as disclosed in the specification, is as a vaccine carrier. The Examiner further asserted that, **in light of this only use**, the specification fails to teach how any antigen-coding gene or any non-antibiotic resistance gene (i.e., as a selectable marker) can be used in the Lac shuttle vector. See the Office Action, page 3, line 17 through page 4, line 14.

Applicants would like to point out that the Examiner erred in asserting that "a vaccine carrier" is the **only use** for a Lac shuttle vector disclosed in the specification. Rather, "a vaccine carrier" is **one of the uses** for a Lac shuttle vector disclosed in the specification. A Lac shuttle vector can also be used for expression of a heterologous or desired gene (see, e.g., page 3, lines 21-25 of the specification) or for selection of a host cell harboring the vector (see, e.g., page 4, lines 1-8 of the specfication). In this connection, Applicants would like to bring to the Examiner's attention that:

> "If multiple uses for claimed compounds or compositions are disclosed in the application, then an enablement rejection must include an explanation,

> sufficiently supported by the evidence, why the specification fails to enable each disclosed use. In other words, if any use is enabled when multiple uses are disclosed, the application is enabling for the claimed invention." (MPEP 2164.01(c))

Since the Examiner failed to recognize the multiple uses of the claimed Lac shuttle vector and based his rejection solely on one of the uses, this rejection is improper and should be withdrawn.

Further, Applicants have provided (1) guidance as to which heterologous or desired genes (e.g., antigenic genes derived from pathogens or cancers) can be inserted into the multiple cloning site and (2) an example (i.e., β-galactosidase) to demonstrate which non-antibiotic resistance genes can be used as selectable markers. Moreover, as admitted by the Examiner, the skill of an artisan in the subject area is considered to be very high (see the office action dated November 27, 2001, page 6, line 14). Numerous examples can be found in the art to show (1) how to insert a gene of one's choice into an expression cassette and express it (see, e.g., Exhibits A-C attached to the response to the office action dated November 27, 2001) and (2) how to use non-antibiotic resistance genes as selectable markers (see, e.g., Exhibits D-F attached to the response to the office action dated November 27, 2001). It has been well established that "not everything necessary to practice an invention need be disclosed. In fact, what is well-known is best omitted. *In re Buchner*, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991). All that is necessary is that one skilled in the art be able to practice the claimed invention, given the level of knowledge and skill in the art" (MPEP 2164.08). In view of the knowledge in the art and the teachings of the specification, one skilled in the art would know how to make and use the claimed Lac shuttle vector. In other words, claim 1, as well as claims 2-11 dependent from it, is sufficiently enabled. By the same token, claim 12 (drawn to a kit containing a Lac shuttle vector of claim 1) and claim 14 (drawn to a method of selecting a host cell harboring a Lac shuttle vector of claim 1) are also enabled.

II

Claim 13 remains rejected by the Examiner for lack of enablement. See the Office Action, page 5, line 14 through page 6, line 21.

Claim 13, as amended, is drawn to a DNA vaccine composition containing a Lac shuttle vector that includes various regulatory sequences, an antigenic gene, a lactic acid bacterial plasmid sequence, and a non-antibiotic marker gene.

In their response to the office action dated November 27, 2001, Applicants submitted a Declaration of Dr. Wei-Yu Lo under 37 C.F.R. § 1.132. Dr. Lo's Declaration provided experimental data showing that immunization of mice with Lactobacillus casei (transformed with a Lac shuttle vector containing an AFP gene) generated strong AFP-specific immune responses. Applicants also submitted a reference (Exhibit G attached to the just-mentioned response to show that the immune response induced by AFP results in protection against AFP-producing murine tumors.

However, the Examiner asserted that Applicants' response was not persuasive

> "because claims are directed to the use of any gene in the Lac shuttle vector of the invention and AFP is not considered enabling for the full scope of the claimed invention, which encompasses any desired gene and is not considered enabling for all antigenic genes. Further, the specification does not contemplate using the AFP gene in the Lac shuttle vector of the instant case, and thus does not provide specific teachings for carrying out the experiments described in the declaration."

The Examiner further asserted that:

> "[T]he purpose of constructing the Lac vector is to use it as DNA vaccine carrier ... by inserting DNA encoding antigens of pathogens and cancer in the eukaryotic expression cassette of the said vector which, when administered to organisms, is expected to generate a protective immune response to a particular antigen and to prevent disease in organisms.
> The specification does not provide an enabling disclosure for the prevention of any and all diseases by administering the said Lac vector. In particular, the specification fails to provide sufficient guidance as to the level and character of immune responses required to achieve a prophylactic effect on any and all diseases. At the time of filing the art recognized that while many immunization strategies using specific antigens were capable of generating an immune response against the particular antigen, few were capable of generating a protective immune response against infections or diseases associated with the immunizing antigen."

The Examiner thus concluded:

> "[B]ased on the lack of guidance in the specification as to the level and character of immune responses required to achieve a prophylactic effect on any and all

> diseases using the instant methodology, the art recognized unpredictability of protecting against any and all diseases, particularly HIV and cancer, using gene therapy, and the breadth of the claims, it would have required undue experimentation for the skilled artisan at the time of filling to practice the full scope of the instant invention as claimed in claim 13."

Applicants would like to point out again that not everything necessary to practice an invention need be disclosed and all that is necessary is that one skilled in the art be able to practice the claimed invention, given the level of knowledge and skill in the art. Genes encoding antigens capable of inducing immune responses against diseases can be found in the art. For example, AFP is one of such genes. Methods of determining the efficacy of a vaccine are also known in the art. See, e.g., Exhibit G attached to the response to the office action dated November 27, 2001, page 3065, left column, last two lines through page 3066, left column, line 12. Another well-known example of an antigen-encoding gene is the hepatitis B virus surface antigen (HBsAg) gene. Mice immunized with plasmids containing the HBsAg gene developed both humoral and cellular immune responses against HBsAg. See, e.g., Chow et al. (1997) J. Virol. 71(1):169-178, a copy of which is attached hereto as "Exhibit A." Further, when challenged with HBsAg-expressing syngeneic tumor cells, significant reduction of tumor growth was observed in mice immunized with plasmids containing the HBsAg gene. See, e.g., Chow et al. (1998) J. Immunol. 160:1320-1329, a copy of which is attached hereto as "Exhibit B." Although some genes may encode antigens unable to induce protective immune responses, presence of these genes does not constitute a sufficient ground for non-enablement rejection. As pointed out by the courts,

> the presence of inoperative embodiments within the scope of a claim does not necessarily render a claim nonenabled. The standard is whether a skilled person could determine which embodiments that were conceived, but not yet made, would be inoperative or operative with expenditure of no more effort than is normally required in the art. See, e.g., *Atlas Powder Co. v. E.I. du Pont de Nemours & Co.*, 750 F.2d 1569, 1577, 224 USPQ 409, 414 (Fed. Cir. 1984).

As mentioned above, whether a Lac shuttle vector carrying a gene encoding an antigen would be effective in inducing a protective immune response can be evaluated based on the knowledge and methods well known in the art. As no undue experimentation is needed, claim 13 is enabled.

Rejection under 35 U.S.C. § 112, second paragraph

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Claim 1, step (b) remains rejected by the Examiner as being indefinite. However, the Examiner gave no reason to support this rejection. See the Office Action, page 2, last line.

In the office action dated November 27, 2001, the Examiner rejected claim 1, step (b) as being indefinite by reciting a term "heterologous." The Examiner asserted that it is unclear whether it is heterologous in relation to E. coli, Lactobacillus, or eukaryotic genome. Applicants believe that they have overcame this rejection by replacing the term "heterologous" with "desired." "Desired gene," as now recited in claim 1, step (b), refers to any gene of one's choice. It has been held that where well-known language conventionally used in the art to which the invention pertains is employed, such is not objectionable under 35 U.S.C. § 112, second paragraph, since one of ordinary skill in the art would be apprised of the scope of the claim in view of the terminology used. See, e.g., *In re Kamal*, 158 USPQ 320, 322 (CCPA 1968). As a skilled person in the art would know which gene to use to meet his or her needs, step (b) of claim 1 is definite, and the rejection should be withdrawn.

II

Claims 12 and 14 are rejected by the Examiner as being indefinite on new grounds. Specifically, the Examiner asserted that "a host cell which" recited in claim 12, step (b) and "conditions which lactose" recited in claim 14, step (ii) are indefinite. The Examiner further asserted that the meaning of "gene thereof is not capable of producing a normal enzymatic function" is not clear. See the Office Action, page 7, "New Grounds of Rejection."

Pursuant to the Examiner's suggestions, Applicants have amended claim 12, step (b) to recite "a host cell in which" and claim 14, step (ii) to recite "conditions in which lactose." Also, Applicants have replaced "gene thereof is not capable of producing a normal enzymatic function" recited in claims 10, 12, and 14 with "gene thereof is non-functional."

For the reasons set forth above, Applicants submit that claims 12 and 14, as amended, particularly point out and distinctly claim the subject matter which Applicants regard as their invention. Thus, the rejection has been overcome and should be withdrawn.

CONCLUSION

Applicants submit that the grounds for rejection asserted by the Examiner have been overcome, and that claims 1-14, as pending, define subject matter that is definite and enabled. On this basis, it is submitted that allowance of this application is proper, and early favorable action is solicited.

Attached is a marked-up version of the changes being made by the current amendment.

Enclosed is a $55 check for the One-Month Petition for Extension of Time fee. Please apply any other charges to Deposit Account No. 06-1050, referencing Attorney Docket No. 12875-002001.

Respectfully submitted,

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Version with markings to show changes made

In the claims:

Claims 10, 12, 13, and 14 have been amended as follows:

10. The Lac shuttle vector as claimed in claim 1, wherein the host cell being transformed is a Gram-positive bacterium, and the endogenous β-galactosidase gene of the host cell is [not capable of producing a normal enzymatic function] non-functional.

12. A kit for expression of a gene, comprising:

(a) the Lac shuttle vector as claimed in claim 1;

(b) a host cell in which the endogenous β-galactosidase gene thereof is [not capable of producing a normal enzymatic function] non-functional; and

(c) [an] a eukaryotic cell.

13. A DNA vaccine composition comprising [the] a Lac shuttle vector [as claimed in claim 1] that contains:

(a) a region which regulates a plasmid copy number, wherein said region comprises an E.coli replication origin sequence;

(b) a eukaryotic gene expression cassette, which comprises a eukaryotic gene transcriptional promoter sequence, a multiple cloning site and a transcriptional terminator sequence, wherein an antigenic gene is inserted into said multiple cloning site;

(c) a lactic acid bacteria plasmid sequence, which comprises a plus origin of replication, and a nucleic acid sequence encoding a protein which is involved in replication of the lactic acid bacteria plasmid; and

(d) a marker gene that is not an antibiotic resistance gene and the promoter sequence thereof.

14. A method for selection of a host cell containing a vector, comprising:

(i) introducing into said host cell the Lac shuttle vector as claimed in claim 1,

wherein the endogenous β-galactosidase gene of said host cell is [not capable of producing a normal enzymatic function] non-functional; and

(ii) culturing said host cell transformed in step (i) under conditions in which lactose is the only carbon source,

thereby selecting a host cell comprising Lac shuttle vector of claim 1.